



PATENT
1110-0279P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Yoshiyuki UENO Conf.: 3959
Appl. No.: 09/700,338 Group: 1648
Filed: November 14, 2000 Examiner: U. Winkler
For: PREVENTIVES/REMEDIES FOR HEPATIC
CIRRHOSIS

REPLY UNDER 37 C.F.R. §1.111

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

May 14, 2004

Sir:

In reply to the Advisory Action issued April 19, 2004, and further to the previously un-entered amendment filed on March 15, 2004 (entry of which has been requested with the filing of the present Request for Continued Examination), the following remarks are respectfully submitted in connection with the above-identified application.

The present response contains remarks.

REMARKS

Claims 8 and 10-18 are pending in the application, with claim 8 being amended and new claims 17 and 18 being added.

Response to Advisory Action of April 19, 2004

In the Advisory Action of April 19, 2004, the Examiner indicates that the amendments of March 15, 2004 were not entered because they raised new issues for consideration and added additional claims without canceling an equal or greater number of claims. Applicants hereby request entry and consideration of the March 15, 2004 amendments and remarks.

In addition, the following remarks are submitted in response to the comments of page 2 of the April 19, 2004 Advisory Action.

1) In the substantive analysis on page 2 of the Advisory Action, the Examiner states that the arguments of March 15, 2004 "are essentially of record." Applicants respectfully disagree with the Examiner on this point. In the Advisory Action issued January 28, 2004, in response to the November 17, 2003 response, the Examiner clearly stated that she only considered references that have publication dates after Harada et al. and Kondo et al. as probative evidence of patentability of the invention. See page 2, lines 5-6 of the Advisory Action which states, "only those references that have publication dates post the Harada et al. or

the Kondo et al. reference cited Office in the 35 U.S.C. §103 rejection have been evaluated." The Examiner's position was that work published prior to Kondo et al. and Harada et al. may not reflect the state of the art at the time of Harada et al. and Kondo et al.

Based on the Examiner's statement in the Advisory Action, Applicants presume that neither Leithäuser et al. (1993) nor Hiramatsu et al. (1994), which both predate the prior art relied upon for the rejection, were evaluated by the Examiner or considered for their probative value.

The arguments of the response of March 15, 2004 are not the same as those previously of record. In the March 15, 2004 response, Applicants rebutted the Examiner's position regarding the probative value of Leithäuser et al. (1993) and Hiramatsu et al. (1994). Applicants demonstrated that the work of Leithäuser et al. (1993) and Hiramatsu et al. (1994) were still accepted as reputable and reliable in 1997 (the time of publication of Harada et al.) and thus should be considered as evidence in support of patentability.

2) The Examiner further asserts on page 2 of the Advisory Action that the findings of Graham et al. do not contradict those of Harada et al. The Examiner appears to take the position that the only relevant teaching of Graham et al. is that PBC cells express Fas/CD95. However, the Examiner appears to fail to

consider that the teaching in Harada et al. that Fas/CD95 is not found on normal liver and is up-regulated on PBC is contradictory to the report in Graham et al. that Fas/CD95 may be expressed on normal liver and there is no change with PBC cells. Further contradictory to the teachings of Harada et al. is are the unequivocal statements in Graham et al. that "a Fas-mediated mechanism is unlikely in view of the low expression we have seen" (page 556, column 2, line 4-6) and that "intervention of apoptosis is unlikely to be a therapeutic target in the treatment of PBC" (page 556, final sentence). Thus, Harada et al. and Graham et al. contradict each other in both the reported expression of Fas on normal versus PBC cells and the possible involvement of a Fas mechanism in PBC. Review and reconsideration of this point by the Examiner is respectfully requested.

3) In the second paragraph of the Advisory Action, the Examiner notes that the claims are drawn to a method of preventing or treating hepatic cirrhosis or bile duct disappearance syndrome. The Examiner's statement is presumably based on the refusal to enter the amendments. Reconsideration of this point upon entry the March 15, 2004 amendments is respectfully requested.

As noted previously, one skilled in the art would have no expectation of success or be motivated to achieve the invention from the teachings of the prior art. The present invention is

therefore not obvious over the cited references and withdrawal of the rejection is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at the telephone number below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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